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L4: Entry 8 of 18 File: USPT Jun 29, 1999

DOCUMENT-IDENTIFIER: US 5916869 A
TITLE: Method of treating birds in ovo

Abstract Text (1):
Methods are disclosed for administering Peptide YY (PYY) receptor agonists to birds in ovo to promote altricial development of the intestinal tract of neonatal birds. Enhanced altricial development of the small intestine in hatchling birds results in an increased absorption of nutrients from the small intestine without a concomitant increase in energy expenditure, thereby resulting in an improved efficiency of nutrient utilization, enhanced rate of post-hatch growth, and reduced post-hatch mortality rate in PYY-treated birds.

Brief Summary Text (8):
Recently, Croom and colleagues have demonstrated that the exogenous administration of epidermal growth factor (EGF) and Peptide YY (PYY) increases glucose absorption in young growing mice. Bird et al., J. Anim. Sci., 2523 (1996); Bird et al., J. Nutr. 124, 231 (1994). Both of these peptides are active orally. PYY has previously been shown to delay gastric emptying and intestinal transit time and to decrease pancreatic enzyme secretion. Savage et al., Gut, 28, 166 (1987); Pironi et al., Gastroenterology 105, 733 (1993); Adrian et al. Gastroenterology 89, 494 (1985). Of particular interest is the ability of PYY to increase glucose absorption without corresponding increases in the energetic cost of digestion. Bird et al., J. Anim. Sci., 2523 (1996). This should result in an increase in net energy absorbed. This technology is currently the subject of co-pending U.S. patent application No. 08/379,354 to Croom et al. Other scientists have shown that both EGF and PYY increase intestinal absorption of amino acids (Schwartz and Storozuk, Amer. J. Surg. 155, 18 (1988)) and fat (Kalogeris et al., Gastro. 110, A809 (1996)).

Brief Summary Text (12):
As a first aspect, the present invention provides a method of enhancing the growth of a bird comprising administration of a Peptide YY (PYY) receptor agonist to a bird in ovo and then incubating the bird to hatch, wherein the PYY receptor agonist is administered in ovo in an amount effective to enhance the growth of the bird.

Detailed Description Text (2):
The present inventors have previously found that exogenously administered Peptide YY (PYY) not only increases nutrient transport across the intestinal absorptive epithelial cell (enterocyte) luminal membrane, the transport is increased without a concomitant increase in energy expenditure by the intestinal tract, as described in co-pending U.S. patent application No. 08/379,354 to Croom et al. As disclosed herein, in ovo administration of PYY to birds results in increased nutrient transport across the small intestine, with a resulting increase in growth, improved efficiency of nutrient utilization, and decreased mortality in the bird after hatch.

Detailed Description Text (7):
As used herein growth and growth enhancement refer to increases in either, or both, weight and size (e.g., height, width, diameter, circumference, etc.) over that which would otherwise occur without PYY treatment. Growth can refer to an increase in the mass (e.g., weight or size) of the entire animal or of a particular tissue (e.g., muscle tissue in general or a specific muscle). Alternatively, growth can indicate a relative increase in the mass of one tissue in relation to another, in particular, an increase in muscle tissue relative to other tissues (e.g., adipose tissue).

Detailed Description Text (8):
As used herein, improving the efficiency of feed utilization refers to a reduction in the Feed Conversion Ratio (FCR) as compared with that which would otherwise occur without PYY treatment. In ovo treatment of birds with PYY improves the FCR for growth

by increasing gastrointestinal nutrient absorption without a concomitant increase in intestinal energy expenditure, thereby increasing the growth efficiency of the neonatal bird.

Detailed Description Text (10):
In preferred embodiments of the invention, in ovo administration of PYY enhances gastrointestinal absorption, improves the efficiency of feed utilization, enhances growth, or reduces mortality in birds one week after hatch. Alternatively, in other preferred embodiments, in ovo administration of PYY enhances gastrointestinal absorption, improves the efficiency of feed utilization, enhances growth, or reduces mortality in birds at two, three, four, six, eight and fifteen weeks after hatch. In yet other preferred embodiments of the invention, in ovo administration of PYY to a bird increases hatchability (i.e., the percentage of birds that hatch and survive).

Detailed Description Text (12):
The present invention may be carried out in any avian species, including, but not limited to chickens, turkeys, ducks, geese, quail, and pheasant, preferably chickens and turkeys. The PYY peptide and PYY agonists used in the methods of the present invention increase feed utilization efficiency in birds by increasing nutrient uptake by the hatchling bird without a concomitant increase in intestinal energy expenditure, thereby increasing the efficiency of post-hatch growth.

Detailed Description Text (18):
PYY (Peptide tyrosine tyrosine) is a 36 amino acid peptide hormone produced by "L type" endocrine cells. See Boucher et al., Regul. Pept. 13, 283 (1986). PYY is a member of the pancreatic polypeptide family, which includes pancreatic polypeptide (PP) and neuropeptide Y (NPY), in addition to Peptide YY. PPY is released in response to feeding and has a variety of effects on the gastrointestinal tract, including inhibition of gastric acid secretion, inhibition of pancreatic exocrine secretion, delay of gastric emptying, and slowing of intestinal transit. See Savage et al., Gut 28, 166 (1987); Pironi et al., Gastroenterology 105, 733 (1993); Adrian et al., Gastroenterology 89, 494 (1985).

Detailed Description Text (47):
In some embodiments of the invention, the bird is treated with the active compound, as described above, both in ovo and after hatch. In formulations of the active compounds of the present invention for administration to birds post-hatch, the active compound is included in an amount effective to accomplish the intended treatment. In general, PYY and its agonists are included in an effective nutrient transport stimulating amount; PYY antagonists are included in an effective nutrient transport inhibiting amount. Alternately, the PYY receptor agonist is included in an amount effective to enhance growth, improve the efficiency of feed utilization, or reduce mortality in a bird after hatch.

Detailed Description Text (58):
In ovo Administration of PYY Improves Growth and FCR of Broiler Chicks

Detailed Description Text (61):
Chicks from eggs treated in ovo with PYY were heavier and had better FCR than broiler chicks from eggs treated in ovo with saline. These data suggest that absorption of glucose and other nutrients can be rate-limiting for growth and feed efficiency in domestic livestock and poultry as proposed by Croom et al. (J. Dairy Sci., 76:2112, 1993). Moreover, in ovo administration of PYY improves both chick growth and feed efficiency, suggesting that PYY enhances precocial development of the small intestine in hatchling chicks, thereby improving net absorption of nutrients and efficiency of nutrient utilization.

Detailed Description Text (78):
The optimal dose of PYY to be administered in ovo to turkeys for post-hatch growth and FCR is evaluated by measuring these parameters, as described in Example 1, following treatment of turkey poults in ovo over a range of PYY concentrations.

Other Reference Publication (11):
Adrian et al.; "Effect of Peptide YY on Gastric, Pancreatic, and Bilary Function in Humans"; Gastroenterology, 89:494-499 (1985).

CLAIMS:

1. A method of enhancing the growth of a bird comprising:

(a) administering a Peptide YY (PYY) receptor agonist to a bird in ovo; and then

(b) incubating said bird to hatch,

wherein said PYY receptor agonist is administered in ovo in an amount effective to enhance the growth of said bird.

36. A method of enhancing the growth of a bird comprising:

(a) administering a Peptide YY (PYY) receptor agonist selected from the group consisting of PYY or a truncated PYY to a bird in ovo; and then

(b) incubating said bird to hatch,

wherein said PYY receptor agonist is administered in ovo in an amount effective to enhance the growth of said bird.

43. A method of enhancing the growth of a bird comprising:

(a) administering Peptide YY (PYY) to a bird in ovo; and then (b) incubating said bird to hatch,

wherein said PYY is administered in ovo in an amount effective to enhance the growth of said bird.

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L2: Entry 3 of 10 File: USPT Apr 4, 2000

DOCUMENT-IDENTIFIER: US 6046167 A
TITLE: Peptide YY analogs

Brief Summary Text (5):
In addition, PYY has been implicated in a number of physiological activities including nutrient uptake (see, e.g., Bilcheik et al. Digestive Disease Week 506:623, 1993), cell proliferation (see, e.g., Laburthe, Trends Endocrinol. Metab. 1:168, 1990; Voisin et al. J. Biol. Chem, 1993), lipolysis (see, e.g., Valet et al., J. Clin. Invest. 85:291, 1990), and vasoconstriction (see, e.g., Lundberg et al., Proc. Natl. Acad. Sci., USA 79:4471, 1982).

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1: J Biol Chem 1993 Sep 25;268(27):20547-54 Related Articles, Links

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Peptide YY receptors in the proximal tubule PKSV-PCT cell line derived from transgenic mice. Relation with cell growth.

Voisin T, Bens M, Cluzeaud F, Vandewalle A, Laburthe M.

Unite de Biologie et Physiologie des Cellules Digestives, Institut National de la Sante et de la Recherche Medicale, Unite 239, Paris, France.

Receptors for peptide YY (PYY) were identified in the PKSV-PCT renal proximal tubule cell line, derived from transgenic mice (SV40 large T antigen under the control of the rat L-type pyruvate kinase 5'-regulatory sequence). Binding of [125I-Tyr36]monoiodo-PYY ([125I] PYY to cell was specific, saturable, and reversible. The order of potency for peptides for inhibiting [125I]PYY binding was: PYY > neuropeptide Y (NPY) = PYY (13-36) >> pancreatic polypeptide. A single class of receptors was observed with a Kd of 0.37 +/- 0.05 nM and a Bmax of 103 +/- 10 fmol/mg protein. After cross-linking, electrophoresis of covalent [125I]PYY-receptor complexes revealed a single band of M(r) 50,000. PYY receptors were exclusively present at the basolateral membrane surface of polarized cells and were coupled negatively to adenylylcyclase by a pertussis toxin-sensitive G protein. PKSV-PCT cell growth and T antigen expression could be modulated by D-glucose in the medium. PYY receptors were exclusively expressed in proliferative cells cultured in the presence of D-glucose. PYY receptors disappeared in the absence of D-glucose and were expressed again when proliferation was activated by reintroduction of D-glucose. PYY stimulated cell growth (17-26% increase) and promoted [methyl-3H]thymidine incorporation into DNA (64% increase; ED50 = 5 nM PYY) of cells grown in D-glucose-enriched medium. This latter effect of PYY was largely reversed by pretreatment of cells with pertussis toxin. These findings suggest that PYY receptors play a role in epithelial cell growth.

PMID: 8397209 [PubMed - indexed for MEDLINE]

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5 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2000:15020 CAPLUS
DN 132:161649
TI Peptide YY exhibits mitogenic effect on **pancreatic** ductal cells while improving acute **pancreatitis**
AU Towfigh, Shirin; Heisler, Tracy; Simon, Natalie; McFadden, David W.
CS Department of Surgery, University of California, Los Angeles, Los Angeles, CA, USA
SO Surgical Forum (1999), 50, 25-27
CODEN: SUFOAX; ISSN: 0071-8041
PB American College of Surgeons
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB The **pancreatic** ductal cell line ARIP was culture in the presence of caerulein, which induces **pancreatitis**, and/or peptide YY (**PYY**). Cells treated with **PYY** had increased growth compared with control and caerulein-treated cells. Caerulein added to cells pretreated with **PYY** resulted in significant growth compared with control, but less that with **PYY** alone. **PYY**-treated cells showed decreased amylase secretion compared with the control and caerulein alone. The combination treatment group also had a significant decrease in amylase prodn. compared with control, decreasing the response seen with caerulein alone. Further studies to explore the mechanism of **PYY**'s mitogenic properties on ductal cells as well as its protective effects on acute **pancreatitis** are underway.
ST peptide YY **pancreas** duct cell **proliferation** **pancreatitis**; amylase **pancreas** peptide YY
IT Animal cell line
(ARIP; peptide YY exhibits mitogenic effect on **pancreatic** ductal cells while improving acute **pancreatitis**)
IT **Pancreas**, disease
(acute **pancreatitis**; peptide YY exhibits mitogenic effect on **pancreatic** ductal cells while improving acute **pancreatitis**)
IT **Pancreas**
(duct; peptide YY exhibits mitogenic effect on **pancreatic** ductal cells while improving acute **pancreatitis**)
IT Cell **proliferation**
(peptide YY exhibits mitogenic effect on **pancreatic** ductal cells while improving acute **pancreatitis**)
IT 106388-42-5, Peptide YY
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide YY exhibits mitogenic effect on **pancreatic** ductal cells while improving acute **pancreatitis**)
IT 9000-92-4, Amylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptide YY exhibits mitogenic effect on **pancreatic** ductal cells while improving acute **pancreatitis**)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

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1: Pfeifer M, Minne HW.

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Vitamin D and Hip Fracture.

Trends Endocrinol Metab. 1999 Dec;10(10):417-420.
PMID: 10542400 [PubMed - as supplied by publisher]

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60/119,577 10 February 1999 (10.02.99) US

(71) Applicant *(for all designated States except US)*: ONTOGENY, INC. [US/US]; 45 Moulton Street, Cambridge, MA 02138 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: PANG, Kevin [US/US]; 45 Moulton Street, Cambridge, MA 02138 (US). LU, Huang–hui [US/US]; 45 Moulton Street, Cambridge, MA 02138 (US).

(74) Agents: VINCENT, Matthew, P. et al.; Foley, Hoag & Eliot, LLP, One Post Office Square, Boston, MA 02109 (US).

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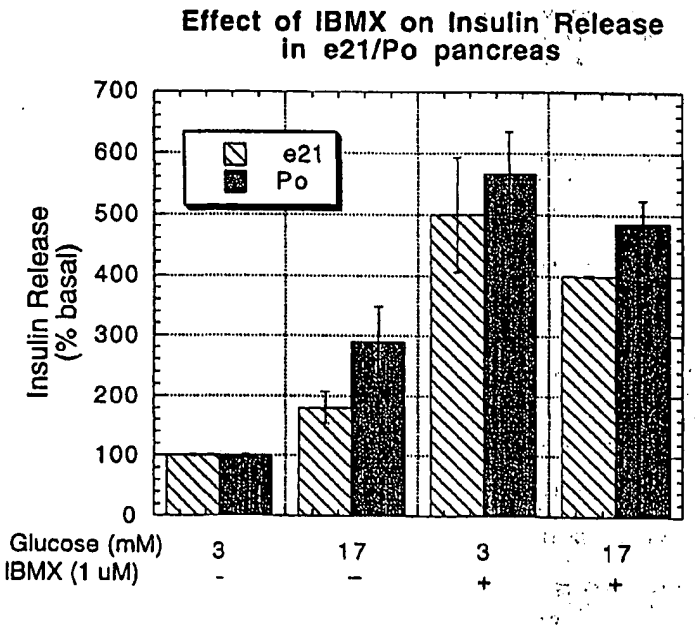
(54) Title: METHODS AND REAGENTS FOR TREATING GLUCOSE METABOLIC DISORDERS



(57) Abstract

The invention relates to methods for potentiating, enhancing or restoring glucose responsivity in pancreatic islets or cells. The methods can be used as therapies for diseases caused by, or coincident with aberrant glucose metabolism, such as Type II Diabetes Mellitus.

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L2: Entry 6 of 6 File: DWPI Aug 17, 2000

DERWENT-ACC-NO: 2000-565257
DERWENT-WEEK: 200229
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TITLE: Promoting the growth of pancreatic cells and reducing degeneration of pancreatic tissue for treating a disease associated with altered glucose metabolism comprises contacting with a composition including (an agonist of) peptide YY

INVENTOR: LU, H; PANG, K

PRIORITY-DATA: 1999US-119577P (February 10, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200047219 A2	August 17, 2000	E	083	A61K038/00
EP 1189629 A2	March 27, 2002	E	000	A61K038/22
AU 200034868 A	August 29, 2000		000	A61K038/00

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